

28. (New) A method according to claim 25 wherein said label is a secondary label.

29. (New) A method according to claim 28 wherein said secondary label is biotin.

#### REMARKS

Claims 7-29 are pending. Claims 20-29 are new. For the Examiner's convenience, a copy of the "Pending Claims" is appended hereto (Appendix A) and a copy of the "Marked-up Version of the Claims" is also appended hereto (Appendix B). Support for amended claims 15, 16, and 19 is found in the claims as filed. Applicants submit that the amendments contains no new matter, because they merely take out references to claims that are cancelled as drawn to a non-elected invention. Support for the new claims is found in the claims as filed and throughout the specification, see *e.g.* page 21, line 13 through page 23, line 9. No new matter was added. Applicants respectfully request entry of the amendment.

In compliance with the Examiner's request regarding the species election, Applicants submit that claims 7-12, 15-22, and 25-27 read on the elected species.

#### CONCLUSION

Applicants submit that the claims are now in form for allowance. An early notification to that effect is respectfully requested.

Respectfully submitted,

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Appendix A  
Pending Claims

7. A method of detecting a first target sequence comprising a first target domain, a second adjacent target domain and a poly(A) sequence, said method comprising:

- a) hybridizing a first probe comprising:
  - i) an upstream universal priming site (UUP); and
  - ii) a first target-specific sequence substantially complementary to said first target domain;

to said first target domain;

- b) hybridizing a second probe comprising:
  - iii) a second target-specific sequence substantially complementary to said second target domain;
  - iv) a downstream universal priming site (DUP);

wherein at least one of said first and second probes comprises at least a first adapter sequence, said poly(A) sequence remains single-stranded, and said target sequence and said first and second probes form a ligation complex;

- c) contacting said ligation complex with a ligase to form a ligated complex;
- d) contacting said ligated complex with a support comprising a poly(T) sequence, such that said poly(A) sequence hybridizes with said poly(T) sequence;
- e) removing unhybridized first and second probe sequences;
- f) denaturing said ligation complex;
- g) amplifying the ligated first and second probes to generate a plurality of amplicons;
- h) contacting said amplicons with an array of capture probes to form assay complexes; and
- i) detecting said assay complexes.

8. A method according to claim 7 wherein said first target domain and said second target domain are directly adjacent.

9. A method according to claim 7 wherein said first target domain and said second target domain are separated by at least one base and said method further includes contacting said ligation complex with a polymerase and at least one dNTP.

10. (Amended) A method according to claim 7, 8 or 9 wherein one of said first and second probes comprises a label.
11. A method according to claim 10 wherein said label is a primary label.
12. A method according to claim 11 wherein said label is a fluorescent label.
13. A method according to claim 10 wherein said label is a secondary label.
14. A method according to claim 13 wherein said secondary label is biotin.
15. (Amended) A method according to claim 7, 8 or 9 wherein said amplifying is done by:
  - a) hybridizing a first universal primer to said UUP;
  - b) providing a polymerase and dNTPs such that said first universal primer is extended;
  - c) hybridizing a second universal primer to said DUP;
  - d) providing a polymerase and dNTPs such that said second universal primer is extended; and
  - e) repeating steps a) through d).
16. (Amended) A method according to claim 7 wherein said array comprises:
  - a) a substrate with a patterned surface comprising discrete sites; and
  - b) a population of microspheres comprising at least a first subpopulation comprising a first capture probe and a second subpopulation comprising a second capture probe.
17. A method according to claim 16 wherein said discrete sites comprise wells.
18. A method according to claim 16 wherein said substrate comprises a fiber optic bundle.
19. (Amended) A method according to claim 7, 8 or 9 wherein said support comprising a poly(T) sequence comprises magnetic beads.
20. (New) A method according to claim 15 wherein at least one of said first universal primers and said second universal primer comprises a label.
21. (New) A method according to claim 20 wherein said label is a primary label.
22. (New) A method according to claim 21 wherein said label is a fluorescent label.
23. (New) A method according to claim 20 wherein said label is a secondary label.

24. (New) A method according to claim 23 wherein said label is biotin.
25. (New) A method according to claim 15 wherein said dNTPs comprise a label.
26. (New) A method according to claim 25 wherein said label is a primary label.
27. (New) A method according to claim 26 wherein said label is a fluorescent label.
28. (New) A method according to claim 25 wherein said label is a secondary label.
29. (New) A method according to claim 28 wherein said secondary label is biotin.

## Appendix B

### Marked-up Version of the Claims

Please cancel claims 1-6

7. A method of detecting a first target sequence comprising a first target domain, a second adjacent target domain and a poly(A) sequence, said method comprising:

- a) hybridizing a first probe comprising:
  - i) an upstream universal priming site (UUP); and
  - ii) a first target-specific sequence substantially complementary to said first target domain;

to said first target domain;

- b) hybridizing a second probe comprising:
  - iii) a second target-specific sequence substantially complementary to said second target domain;
  - iv) a downstream universal priming site (DUP);

wherein at least one of said first and second probes comprises at least a first adapter sequence, said poly(A) sequence remains single-stranded, and said target sequence and said first and second probes form a ligation complex;

- c) contacting said ligation complex with a ligase to form a ligated complex;
- d) contacting said ligated complex with a support comprising a poly(T) sequence, such that said poly(A) sequence hybridizes with said poly(T) sequence;
- e) removing unhybridized first and second probe sequences;
- f) denaturing said ligation complex;
- g) amplifying the ligated first and second probes to generate a plurality of amplicons;
- h) contacting said amplicons with an array of capture probes to form assay complexes; and
- i) detecting said assay complexes.

8. A method according to claim 7 wherein said first target domain and said second target domain are directly adjacent.

9. A method according to claim 7 wherein said first target domain and said second target domain are separated by at least one base and said method further includes contacting said ligation complex with a polymerase and at least one dNTP.

10. (Amended) A method according to claim 7, 8 or 9 wherein one of said first and second probes comprises a label.
11. A method according to claim 10 wherein said label is a primary label.
12. A method according to claim 11 wherein said label is a fluorescent label.
13. A method according to claim 10 wherein said label is a secondary label.
14. A method according to claim 13 wherein said secondary label is biotin.
15. (Amended) A method according to claim [1 or] 7, 8 or 9 wherein said amplifying is done by:
- a) hybridizing a first universal primer to said UUP;
  - b) providing a polymerase and dNTPs such that said first universal primer is extended;
  - c) hybridizing a second universal primer to said DUP;
  - d) providing a polymerase and dNTPs such that said second universal primer is extended; and
  - e) repeating steps a) through d).
16. (Amended) A method according to claim [1 or] 7, 8 or 9 wherein said array comprises:
- a) a substrate with a patterned surface comprising discrete sites; and
  - b) a population of microspheres comprising at least a first subpopulation comprising a first capture probe and a second subpopulation comprising a second capture probe.
17. A method according to claim 16 wherein said discrete sites comprise wells.
18. A method according to claim 16 wherein said substrate comprises a fiber optic bundle.
19. (Amended) A method according to claim [1 or] 7, 8 or 9 wherein said support comprising a poly(T) sequence comprises magnetic beads.
- 20. (New) A method according to claim 15 wherein at least one of said first universal primers and said second universal primer comprises a label.
21. (New) A method according to claim 20 wherein said label is a primary label.
22. (New) A method according to claim 21 wherein said label is a fluorescent label.

23. (New) A method according to claim 20 wherein said label is a secondary label.
24. (New) A method according to claim 23 wherein said label is biotin.
25. (New) A method according to claim 15 wherein said dNTPs comprise a label.
26. (New) A method according to claim 25 wherein said label is a primary label.
27. (New) A method according to claim 26 wherein said label is a fluorescent label.
28. (New) A method according to claim 25 wherein said label is a secondary label.
29. (New) A method according to claim 28 wherein said secondary label is biotin.